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(56) **References Cited**

#### U.S. PATENT DOCUMENTS

4,683,198 A	7/1987	Ishikawa et al.
4,919,770 A	4/1990	Preidel et al.
5,054,039 A	10/1991	Blackmon et al.
5,108,564 A	4/1992	Szuminsky et al.
5,801,006 A	9/1998	Kaufman
7,132,270 B2	11/2006	Kratzsch et al.
7,547,535 B2	6/2009	Kratzsch et al.
2005/0023152 A1	2/2005	Surridge et al.
2009/0246808 A1	10/2009	Wilsey et al.

#### FOREIGN PATENT DOCUMENTS

EP	0821234 A2	1/1998
EP	0974303 B2	7/2006
EP	1660648 B1	10/2013

WO	1998/033936 A1	8/1998
WO	2001/049247 A2	7/2001
WO	2005/045016 A2	5/2005
WO	2007/012494 A1	2/2007
WO	2007/071562 A1	6/2007
WO	2009/103540 A1	8/2009
WO	2009/118157 A1	10/2009
WO	2014/001382 A1	1/2014

#### OTHER PUBLICATIONS

Baik, Sang-Ho et al., Cooperative Effect of Two Surface Amino Acid Mutations (Q252L and E170K) in Glucose Dehydrogenase from *Bacillus megaterium* IWG3 on Stabilization of Its Oligomeric State, *Applied and Environmental Microbiology*, 2005, pp. 3285-3293, vol. 71, No. 6.

Bünemann, H. et al., Synthesis and Properties of Acrylamide-Substituted Base Pair Specific Dyes for Deoxyribonucleic Acid Template Mediated Synthesis of Dye Polymers, *Biochemistry*, 1981, pp. 2864-2874, vol. 20, No. 10.

Cooney, M. J. et al., Enzyme catalysed biofuel cells, *Energy & Environmental Science*, 2008, pp. 320-337, vol. 1.

Ghosh, R. and Quayle, J. R., Phenazine Ethosulfate as a Preferred Electron Acceptor to Phenazine Methosulfate in Dye-Linked Enzyme Assays, *Analytical Biochemistry*, 1979, pp. 112-117, vol. 99.

Habermüller, Katja et al., Electron-transfer mechanisms in amperometric biosensors, *Fresenius Journal of Analytical Chemistry*, 2000, pp. 560-568, vol. 366.

Heller, Adam and Feldman, Ben, *Electrochemical Glucose Sensors and Their Applications in Diabetes Management*, Chemical Reviews, 2008, pp. 2482-2505, vol. 108.

Hisada, Ryuki et al., Photochemical Stabilities and Biochemical Reactivities of Some Derivatives of 5-Methylphenazinium Methyl Sulfate (Phenazine Methosulfate), *Journal of Applied Biochemistry*, 1981, pp. 535-543, vol. 3.

Hutchinson, Edward J. et al., Synthesis of carbocyclic NAD<sup>+</sup> containing a methylenebisphosphonate linkage for the investigation of ADP-ribosyl cyclase, *Chemical Communications*, 1996, pp. 2765-2766, vol. 24.

Hönes, Joachim et al., *The Technology Behind Glucose Meters: Test Strips, Diabetes Technology & Therapeutics*, 2008, pp. S-10-S-26, vol. 10, Supplement 1.

International Search Report dated Jun. 1, 2015, in Application No. PCT/EP2015/057933, 4 pages.

Inzelt, G. and Puskás, Z., Adsorption and precipitation during the redox transformations of phenazine, *Electrochimica Acta*, 2004, pp. 1969-1980, vol. 49.

(Continued)

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(57) **ABSTRACT**

The present invention relates to a chemical compound or a salt or solvate thereof being an 1-amino-phenazine derivative and to uses thereof. The present invention further relates to a chemistry matrix and to a test element comprising the aforesaid chemical compound. Moreover, the present invention relates to a method for determining the amount of an analyte in a sample, comprising contacting said sample with a chemistry matrix according to the present invention, estimating the amount of electrons liberated or consumed by the chemistry matrix in the presence of said liquid sample, and thereby determining the amount of an analyte in a liquid sample.

**15 Claims, 5 Drawing Sheets**